

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2005/006082

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07H17/00 C07H17/08 A61K31/7048 A61K31/7052 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/013153 A (ZAMBON GROUP S.P.A; NAPOLETANO, MAURO; MORIGGI, ERMANNO; MEREU, ANDREA) 12 February 2004 (2004-02-12) see in particular compounds 5, 7, 8, 30 -----	1-3, 5-31
X	WO 00/40589 A (PLIVA, FARMACEUTSKA INDUSTRIJA. DIONI&CCARON; BUREK, GORDANA; LAZAREVS) 13 July 2000 (2000-07-13) claims 2,4,5 -----	1-3, 5-31
X	WO 99/22722 A (ABBOTT LABORATORIES) 14 May 1999 (1999-05-14) see in particular compound 5 -----	1-3, 5-31
X	WO 99/16779 A (ABBOTT LABORATORIES) 8 April 1999 (1999-04-08) page 18 - page 19 -----	1-3, 5-31
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

24 August 2005

Date of mailing of the international search report

23. 11. 2005

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/051855 A (KOSAN BIOSCIENCES, INC) 4 July 2002 (2002-07-04) example 44 -----	1-3,5-31
X	EP 0 643 068 A (CHUGAI SEIYAKU KABUSHIKI KAISHA; CHUGAI PHARMACEUTICAL CO LTD) 15 March 1995 (1995-03-15) page 19 - page 22 -----	1-3,5-31
E	WO 2005/049632 A (RIB-X PHARMACEUTICALS, INC; FARMER, JAY, J; GOLDBERG, JAY, A; OYELERE,) 2 June 2005 (2005-06-02) the whole document -----	1-3,5-31
E	WO 2005/042554 A (RIB-X PHARMACEUTICALS, INC; OYELERE, ADEGBOYEGA, K; FARMER, JAY, J) 12 May 2005 (2005-05-12) the whole document -----	1-3,5-31

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-3, 5-31 (parts)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3,5-31 (parts)

Compounds of formula (I), pharmaceutical compositions containing them, their preparation and use

2. claims: 1-31 (parts)

Compounds of formula (II), pharmaceutical compositions containing them, their preparation and use

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/006082

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004013153	A	12-02-2004	AU 2003269861 A1 BR 0313162 A CA 2493995 A1 CN 1678620 A EP 1529053 A2	23-02-2004 05-07-2005 12-02-2004 05-10-2005 11-05-2005
WO 0040589	A	13-07-2000	AU 3067900 A CA 2358594 A1 CN 1332746 A CZ 20012316 A3 EP 1140962 A2 HK 1043597 A1 HR 980646 A1 HU 0105049 A2 JP 2002534432 T RU 2234510 C2 SK 9182001 A3 US 6573367 B1	24-07-2000 13-07-2000 23-01-2002 17-10-2001 10-10-2001 08-10-2004 28-02-2001 29-04-2002 15-10-2002 20-08-2004 07-01-2002 03-06-2003
WO 9922722	A	14-05-1999	AU 1206799 A BG 104436 A BR 9813318 A CA 2307850 A1 CN 1278178 A EP 1027060 A2 HU 0100012 A2 JP 2001521891 T NO 20002189 A PL 340604 A1 SK 6172000 A3 TR 200001147 T2 ZA 9809885 A	24-05-1999 29-12-2000 22-08-2000 14-05-1999 27-12-2000 16-08-2000 28-05-2001 13-11-2001 28-06-2000 12-02-2001 12-03-2001 21-08-2000 05-05-1999
WO 9916779	A	08-04-1999	AT 260293 T AU 737310 B2 AU 9317698 A BG 104340 A BR 9812577 A CA 2303930 A1 CN 1271363 A DE 69821964 D1 DE 69821964 T2 DK 1025114 T3 EP 1025114 A1 ES 2217579 T3 HU 0004579 A2 JP 2001518476 T NO 20001439 A PL 339575 A1 PT 1025114 T SK 4562000 A3 TR 200000805 T2	15-03-2004 16-08-2001 23-04-1999 31-01-2001 17-10-2000 08-04-1999 25-10-2000 01-04-2004 30-12-2004 05-07-2004 09-08-2000 01-11-2004 28-05-2001 16-10-2001 29-05-2000 18-12-2000 30-07-2004 12-09-2000 23-10-2000
WO 02051855	A	04-07-2002	CA 2429709 A1 EP 1337540 A2 JP 2004522726 T	04-07-2002 27-08-2003 29-07-2004
EP 0643068	A	15-03-1995	AT 169927 T	15-09-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/006082

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0643068	A	AU 659740 B2	25-05-1995
		AU 4089793 A	30-12-1993
		CA 2117883 A1	09-12-1993
		CN 1081184 A	26-01-1994
		DE 69320476 D1	24-09-1998
		DE 69320476 T2	25-03-1999
		DK 643068 T3	08-02-1999
		ES 2120499 T3	01-11-1998
		HK 1009969 A1	12-05-2000
		HR 930926 A1	28-02-1995
		IL 105810 A	27-12-1998
		WO 9324509 A1	09-12-1993
		KR 226311 B1	15-10-1999
		SG 52785 A1	28-09-1998
		SI 9300281 A	31-12-1993
		US 5658888 A	19-08-1997
		ZA 9303679 A	21-12-1993

WO 2005049632	A	02-06-2005	NONE

WO 2005042554	A	12-05-2005	NONE

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/006082

International filing date (day/month/year)
25.02.2005

Priority date (day/month/year)
27.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07H17/00, C07H17/08, A61K31/7048, A61K31/7052, A61P31/04

Applicant
RIB-X PHARMACEUTICALS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application; -
- ☒ claims Nos. 1-3 (parts), 4, 5-31 (parts)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1-3 (parts), 4, 5-31 (parts)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-3 (parts), 5-31 (parts)

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-3,5-31
Inventive step (IS)	Yes: Claims	
	No: Claims	1-3,5-31
Industrial applicability (IA)	Yes: Claims	1-3, 5-19,29-31
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

This report only covers invention (1) (see item iv) below) since the applicants did not pay the search fee for invention (2).

Claims 20-28 relate to medical treatment of the human body and hence to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

The citations are:

D1/ WO 2004/013153 A2

D2/ WO 00/40589 A2

D3/ WO 99/22722 A2

D4/ WO 99/16779 A1

D5/ WO 02/051855 A2

D6/ EP 0 643 068 A1

The application comprises two inventions:

Invention (1):

Compounds of formula (I), pharmaceutical compositions containing them, their preparation and use according to claims 1-3, 5-31

Invention (2):

Compounds of formula (II), pharmaceutical compositions containing them, their preparation and use according to claims 1-31

Compounds according to formula (I) of claim 1 and pharmaceutical formulations containing them are comprised in the state of the art as represented by D1, see compounds 5 (E = CH₂, F = alkyl containing NH; G = thiazolyl), 7, 8, 30, and corresponding "intermediates"; and D2, see claim 2, 4, 5 (E = -C(O)O-, F = CH₂, G = phenyl). The medical use of the compounds taught in D1 is the same as in the application. Also, compounds which are structurally similar to the claimed compounds are disclosed in D3, D4, D5 and D6. They correspond to the proviso vi) and vii) of claim 1 (D3, compound 5 (E = CH₂, G = phenyl); D4 p. 18-19 (E = CH₂, G = cycloalkyl, unsubstituted and substituted aryl); D5, example 44). Given that their medical use is the same as in the application, the subject-matter of the claims with respect to formula (I) is obvious. It appears therefore that formula (I) and formula (II) do not comprise a special technical feature in the sense of Rule 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Invention (1):

The subject-matter of claims 1-3 and 5-31 lacks novelty and inventive step (see item IV above).

Re Item VIII

Certain observations on the international application

The expression "prodrug" used in the claims is a functional expression and not allowable in view of the requirements of Article 6 PCT since a claim related to a group of compounds should define their *structural features* to give a clear understanding of the scope of the claim.

Claim 29 does not specify the technical features of the claimed synthesis and hence contravenes the requirements of Article 6 PCT.